

CLAIMS

- 5 line.
1. A reversibly- or reverse- immortalised olfactory ensheathing glia (OEG) cell
2. A cell line according to claim 1, for use in a method of therapy.
3. A cell line according to claim 2, for use in promoting neuronal regeneration.
- 10 4. A cell line according to any preceding claim, which is a human cell line.
5. A pharmaceutical composition comprising a cell line of any preceding claim,
and a pharmaceutically acceptable carrier.
- 15 6. A method of making a population of functional OEG cells for transplantation
into a patient, which comprises:
- a) providing a sample of primary OEG cells;
- 20 b) immortalizing the OEG cells by transforming the OEG cells with a DNA
construct comprising a removable DNA segment containing an oncogene or
combination of oncogenes, thereby producing immortalised OEG cells;
- c) growing the immortalised OEG cells;
- d) selecting those immortalised OEG clonal cell lines which maintain their
functional properties; and
- 25 e) removing the oncogene or combination of oncogenes from the immortalised
OEG cells, the removal resulting in the production of the population of
functional OEG cells for transplantation into the patient.
- 30 7. The method of claim 6, wherein the OEG cells are obtained from a human
donor.

8. The method of claim 6, wherein the oncogene or combination of oncogenes is made removable by flanking it with recombinase target sites, and the removing is accomplished by introducing into the immortalised cells a gene that is expressed to produce a recombinase that specifically recognizes the recombinase target sites.

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9. The method of claim 8, wherein the recombinase is Cre recombinase and the recombinase target sites are loxP sites.

10. The method of claim 6, wherein the oncogene is the gene encoding SV40 large T antigen, the gene encoding telomerase catalytic subunit, the gene encoding Bmi-1 protein or any combination of said oncogenes.

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11. The method of claim 6, wherein the removable DNA segment further contains a suicide gene, which encodes a gene product that enables destruction of the immortalised cells by an exogenous agent if the removable DNA segment is not removed from the cells.

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12. The method of claim 11, wherein the suicide gene is a gene encoding herpes simplex virus thymidine kinase, and the cells are destroyed by exposure to gancyclovir if the removable DNA segment is not removed from the cells.

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13. A population of functional OEG cells produced by the method of claim 6.

14. A method of treating a patient for neural damage, comprising transplanting into the patient a sufficient quantity of the OEG cells of claim 13 to provide promotion of neuronal regeneration in the neuronal injured region of the patient.

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15. A method of making a population of functional OEG cells for transplanting into a patient, which comprises:

a) providing a sample of primary OEG cells;

b) immortalizing the OEG cells by transforming the OEG cells with a DNA construct comprising a removable DNA segment containing an oncogene or a combination

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of oncogenes, a selectable marker gene, and a gene encoding herpes simplex virus thymidine kinase, the genes together being flanked on either side by loxP sites;

c) growing the immortalised OEG cells;

d) selecting those immortalised OEG clonal cell lines which maintain their functional properties; and

e) reversing the immortalization of the OEG cells by removing the DNA segment from the immortalised OEG cells, the removing being accomplished by introducing into the immortalised OEG cells a gene encoding Cre recombinase to effect excision of the DNA segment at the loxP sites, the excision resulting in the production of the population of functional OEG cells for transplanting into a patient.

16. The method of claim 15, wherein the OEG cells are obtained from a human donor.

17. The method of claim 15, wherein the oncogene is the gene encoding SV40 large T antigen, the gene encoding telomerase catalytic subunit, the gene encoding Bmi-1 protein or any combination of said oncogenes.

18. A population of functional OEG cells produced by the method of claim 10.

19. A method of treating a patient for neural damage, comprising transplanting into the patient a sufficient quantity of the OEG cells of claim 18 to provide promotion of neuronal regeneration in the neuronal injured region of the patient.

20. An immortalised OEG cell comprising a primary OEG cell transformed with a DNA construct comprising two recombinase target sites that flank an oncogene or combination of oncogenes which confers immortalization to the OEG cell, wherein the immortalization is reversible by excision of the oncogene by cleavage at the recombinase target sites when the target sites are exposed to a recombinase that specifically recognizes the target sites.

21. The immortalised OEG cell of claim 20, wherein the recombinase target sites are loxP sites and the immortalization is reversible by Cre recombinase cleavage at the loxP sites.

5 22. The immortalised OEG cell of claim 20, wherein the DNA construct further comprises a selectable marker gene.

23. The immortalised OEG cell of claim 20, wherein the DNA construct further comprises a suicide gene, which encodes a gene product that enables destruction of the
10 immortalised OEG cell by an exogenous agent if the oncogene is not removed from the cells.

24. The immortalised OEG cell of claim 23, wherein the suicide gene is a gene encoding herpes simplex virus thymidine kinase, and the exogenous agent is gancyclovir.

15 25. The immortalised OEG cell of claim 20, wherein the OEG cell is obtained from a human donor.

26. A cell line comprising a population of the immortalised OEG cell of claim 25.

20 27. A reverse-immortalised OEG cell that is functional upon transplantation into a patient, produced by exposing the DNA construct within the immortalised OEG cell of claim 20 to a recombinase that excises the oncogene or combination of oncogenes by cleavage at the recombinase target sites.

25 28. A method of treating a patient for neural damage, comprising transplanting into the patient a sufficient quantity of the reverse-immortalised OEG cells of claim 27 to provide promotion of neuronal regeneration in the neuronal injured region of the patient.

30 29. A cell library comprising a collection of reversibly-immortalized or reverse-immortalised OEG cells prepared according to the methods of any one of claims 6 to 12 or 15 to 17.

30. The use of reversibly- or reverse-immortalised olfactory ensheathing glia cells in the preparation of a medicament for treating neuronal damage.